UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF WEST VIRGINIA
CHARLESTON DIVISION

IN RE: ETHICON, INC., PELVIC REPAIR SYSTEM PRODUCTS LIABILITY LITIGATION	**Master File No. 2:12-MD-02327** **MDL 2327** **JOSEPH R. GOODWIN** **U.S. DISTRICT JUDGE**
THIS DOCUMENT RELATES TO ETHICON WAVE 5 MOTIONS	

PLAINTIFFS' OPPOSITION TO DEFENDANTS' MOTION AND MEMORANDUM IN SUPPORT OF ITS MOTION TO EXCLUDE CERTAIN GENERAL OPINIONS OF JERRY BLAIVAS, M.D.

I. INTRODUCTION

Now come Plaintiffs in response to Defendants' Ethicon, Inc., Ethicon LLC, and Johnson & Johnson (collectively "Ethicon") Motion to Exclude Certain General Opinions of Jerry Blaivas, M.D. ("Dr. Blaivas") (Doc. 4368) ("Ethicon Motion") filed with the Court August 15, 2017, along with the Memorandum in Support (Doc. 4373) ("Ethicon Brief").[1] Ethicon primarily adopts its Wave 4 briefing in challenging the reliability and relevance of Dr. Blaivas's opinions, along with his qualifications. (Eth. Br., 1)(adopting and incorporating by reference Doc. 3589). In addition, Ethicon promulgates an additional challenge to Dr. Blaivas's opinions regarding the Prolift +M device, implanted in Plaintiff Monica Reyes ("Ms. Reyes"). (*Id*. 1-2.) Ethicon claims that Dr. Blaivas's opinions pertinent to the Prolift +M device must be excluded because he has not

[1] Future citations to the Ethicon Brief will be in the form (Eth. Br., ___.)

submitted an expert report specific to the Prolift +M. For reasons of the following, the Ethicon Motion must be denied in full. In support, Plaintiffs now bring the following:

A. PLAINTIFFS ADOPT AND INCORPORATE BY REFERENCE THEIR PREVIOUS BRIEFING IN WAVE 4 OF THIS LITIGATION.

Plaintiffs filed Plaintiffs' Opposition to Defendants' Motion and Memorandum of Law in Support of Its Motion to Exclude Certain General Opinions of [Dr. Blaivas] with the Court on April 27, 2017 (Doc. 3758) ("Plaintiffs' Wave 4 Brief").[2] Plaintiffs now adopt and incorporate by reference, as though fully set forth herein, Plaintiffs' Wave 4 Brief in response to the Ethicon Motion. Dr. Blaivas's expert opinions are fully admissible for the reasons set forth in Plaintiffs' Wave 4 Brief.

B. DR. BLAIVAS'S OPINIONS REGARDING THE PROLIFT +M DEVICE ARE ADMISSIBLE.

In addition, Ethicon seeks to exclude Dr. Blaivas's Prolift +M opinions because he did not submit a specific expert report about the device. (Eth. Br., 1-2.) Ethicon's arguments are unavailing and Dr. Blaivas's opinions should be admitted in full.

As Ethicon is undoubtedly aware, Dr. Blaivas has submitted a number of reports pertinent to Prolift devices, the most recent of which is dated January 17, 2017.[3] This expert report is addressed in Plaintiffs' Wave 4 Brief and Plaintiffs' arguments in support of Dr. Blaivas's Prolift opinions are, therefore, incorporated by reference here. (*Supra*. at Subpart A.)

Also in support, Plaintiffs argue that there is no reason to differentiate between the Prolift +M and the other Prolift products about which Dr. Blaivas proffers his opinions in his previously-submitted reports. (See e.g. Ex. A.) All Prolift devices--of whatever form-- are comprised of

[2] Future Citations to Plaintiffs' Wave 4 Brief will be in the form (Pl. Wave 4 Br., ___.).
[3] Dr. Blaivas's expert report of January 17, 2017 is attached hereto as Exhibit A. Future citations to Exhibit A will be in the form (Ex. A, __.).

polypropylene mesh, which Dr. Blaivas considers to be a "hazardous material to use for vaginal prolapse repairs." (Ex. A, 3, 8-10) (See also Pl. Wave 4 Br., 16-17, 20-21.) In a blatant attempt to favor form over substance, Ethicon now argues that Dr. Blaivas's opinions regarding the Prolift +M must be excluded because they are not the subject of an expert report. However, it is clear that Dr. Blaivas has both submitted reports pertinent to all Prolift products (including the report attached hereto as Exhibit A) and has proffered testimony regarding why he thinks the Prolift devices are not safe. (See Pl. Wave 4 Br., 16-17, 20-21.) Such opinions are broad enough to include the Prolift + M device at issue now. Dr. Blaivas's opinions should be admitted in full and the Ethicon Motion must be denied.

II. CONCLUSION

For the reasons of the foregoing, Dr. Blaivas's general opinions are reliable and should be admitted in full.

Respectfully submitted,

Date: August 28, 2017

By: /s/ Fidelma L. Fitzpatrick

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CERTIFICATE OF SERVICE

I hereby certify that on August 29, 2017, I electronically filed the foregoing document with the Clerk of the court using CM/ECF system which will send notification of such filing to the CM/ECF participants registered to receive service in this MDL.

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EXHIBIT A

UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF WEST VIRGINIA
AT CHARLESTON

IN RE: ETHICON, INC., PELVIC REPAIR SYSTEM PRODUCTS LIABILITY LITIGATION **THIS DOCUMENT RELATES TO ALL WAVE 4 CASES INVOLVING PROLIFT**	**Master File No. 2:12-MD-02327** **JOSEPH R. GOODWIN** **U.S. DISTRICT JUDGE**

RULE 26 EXPERT REPORT OF JERRY G. BLAIVAS

The following report is provided pursuant to Rule 26 of the Federal Rules of Civil Procedure. My opinions are as follows:

I. QUALIFICATIONS

I am a board certified urologist in the state of New York. I attended Tufts College for my bachelor's degree in 1964 and Tufts University School of Medicine for my medical doctorate in 1968. I completed a urology residency in 1976 after completing a general surgery internship followed by a two year general surgery residency. I have been teaching medicine since 1976 at Tufts University School of Medicine, Columbia University, Cornell University and most recently, SUNY Downstate Medical School. Throughout my academic career, I remained a practicing surgeon in a number of hospitals in Massachusetts and New York, and am currently an attending surgeon at The New York Presbyterian Hospital and Lenox Hill Hospital.

I have been a pioneer in the field of female urology, specifically relating to the surgical treatment of female stress urinary incontinence and pelvic organ prolapse. In 1999, I was the recipient of the Lifetime Achievement Award by the Society of Urodynamics and Female Urology (SUFU). This honor was bestowed on me in recognition of my efforts and expertise in the field of urinary incontinence and pelvic organ prolapse. I was the second recipient of the Victor A. Politano Award in 2009. The American Urological Association presents the Victor A. Politano Award annually to an individual in appreciation of their outstanding achievements in the field of urinary incontinence and for enhancing the treatment of incontinent patients." In 2013 I was honored by the Society of Urodynamics and Female Urology as being one of the four "founding fathers" of the new sub-specialty of Female Pelvic Medicine and Reconstructive Surgery. This honor was bestowed on me in recognition of my efforts and expertise in lower urinary tract disorders like incontinence, overactive bladder and pelvic organ prolapse in women. Although I was trained as a urologist, in the mid-1980s, I developed a two team approach to the surgical management of women with incontinence, combining the expertise of the gynecologist expert at vaginal hysterectomy and prolapse repairs with a urologist, myself, expert at incontinence

operations. My goal was for each surgeon, the urologist and the gynecologist to acquire the expertise of the other, so that in the end, only one surgeon would be necessary to perform these complex surgeries. I had already spent some time working with Ted Morgan, a pioneering prolapse and incontinence gynecologic surgeon in Toronto. In New York, at the Presbyterian Hospital, I operated weekly with both Leon Tanzer and Terry Brody, both world renowned gynecologic surgeons. Throughout this period of time, I also collaborated with a number of world renown gynecologic surgeons including David Nichols and George Mitchell.

In the early 1990's, I met with the leaders of the American College of Obstetrics and Gynecology and proposed the formation of a new specialty - urogynecology - combining the expertise of urologists and gynecologists. This was the forme fruste of the sub-specialty of female pelvic medicine and reconstructive surgery. In the mid 1990's, I inaugurated the first ever symposium designed to bring together the expertise of gynecologists and urologists under the auspices of the American Urologic Association. The symposium was named Female Urology and Urogynecology-a Meeting of the Minds. In approximately 1998, Laurie Romanzi, a gynecologist, completed a fellowship under my direction and became the first surgeon that I know of to be trained in both urology and gynecology. In 2002, I began my long collaboration with Mickey Karram who became co-director of the symposium with me.

I have personally managed hundreds of patients with mesh sling and prolapse complications, many resulting from Prolift devices and surgically removed these devices when warranted by complications.

Although I was trained as a urologist, in the mid-1980s, I developed a two-team approach for the surgical management of women with incontinence and pelvic floor problems, combining the expertise of a gynecologist who is an expert in vaginal hysterectomy with a urologist who is an expert in incontinence operations. My goal was for each surgeon, the urologist and the gynecologist, to acquire the expertise of the other, so that in the end, only one surgeon would be necessary to perform these complex surgeries. I had already spent time working with Dr. Ted Morgan, a pioneering prolapse and incontinence gynecologic surgeon in Toronto. In New York, at the Presbyterian Hospital, I operated weekly with both Dr. Leon Tanzer and Dr. Terry Brody, world renowned gynecologic surgeons. Throughout this period of time, I also collaborated with other world renown gynecologic surgeons including David Nichols, Bob Zacharin, and George Mitchell. I the 1990's I inaugurated the first ever symposium designed to bring together the expertise of gynecologists and urologists under the auspices of the American Urologic Association. The symposium was entitled "Female Urology and Urogynecology – A Meeting of the Minds." In 2004, I began my long collaboration with Mickey Karram who became co-director of the symposium. In 2013, I was honored by Society for Urodynamics and Female Urology as one of the four founding "fathers" of the newly recognized sub-specialty Female Pelvic Medicine and Reconstructive Surgery.

I have significant experience with pelvic repair surgery of all types. I have performed thousands of pelvic surgeries for both incontinence and/or prolapse. I have lectured nationally and internationally on these topics. I have personally managed patients with complications resulting from Prolift devices and surgically removed these devices when complications warrant.

II. SUMMARY OF OPINIONS

1. Transvaginal polypropylene mesh kits, like Prolift, used to treat Pelvic Organ Prolapse, cause serious and life-style altering complications including, but not limited to, chronic pelvic pain, dyspareunia, infections, nerve injuries, sexual impairment, bowel and bladder dysfunction, fistulas, and vaginal and visceral erosion. These complications often require reoperation and are sometimes permanent.

2. Inherent properties of polypropylene mesh make it a hazardous material to use for vaginal prolapse repairs. These include chronic inflammation and foreign body reaction, shrinkage/contraction, deformation, bacterial colonization, stiffening, fibrosis and scar plate formation, nerve entrapment, degradation, production of unknown and potentially toxic chemicals, and possible carcinogenesis. The mesh arms of the Prolift devices are placed blindly with trocars into spaces that are densely innervated and vascularized. This placement poses a significant risk for complications including, but not limited to, dyspareunia, pain, vaginal scarring and deformation, and shrinkage/contraction.

3. Removal of the Prolift device is extremely difficult, if not impossible with a high likelihood of injuring other structures, particularly the bladder and rectum and failing to alleviate symptoms, especially those related to pain and dyspareunia. In most instances, remnants of mesh remain after removal attempts.

4. Because of risks of removal surgery and unknown best practices, surgeons may elect to do an incomplete operation, subjecting the patient to poor results or further surgery.

5. These serious complications may occur even in experienced hands and when proper surgical technique is used.

6. Prolift procedures are not “minimally invasive.”

7. The incidence of these complications is unacceptably high.

8. Appropriate and unbiased clinical testing, if performed, would have shown the problems and complications associated with polypropylene mesh kits.

9. Ethicon should have had a high level of suspicion as to the performance of the Prolift devices based on predicate products.

10. Ethicon’s warnings were inaccurate and misleading and did not provide physicians with the information needed to make responsible decisions and obtain informed consent from patients.

11. The Prolift devices are defective from a clinical standpoint. Flaws in the design include, but are not limited to, the choice of material, the blind trocar-based insertion method, the

presence of arms with sharp edges implanted in high-risk areas, high complication rates, and the inability to remove.

12. Ethicon marketed these products to inadequately trained physicians.

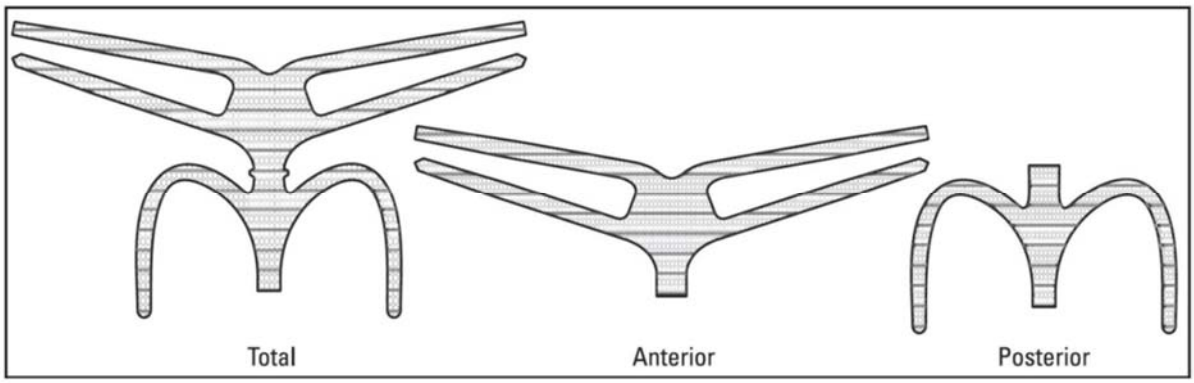
13. There are alternative procedures that are safer and equally or more effective.

14. The risks of the Prolift devices outweigh any benefits.

15. Through the Pelvic Health Coalition, Ethicon joined forces with other mesh manufacturers to influence reimbursement of mesh procedures through false and misleading information and in complete disregard to patient safety.

III. DESCRIPTION OF THE DEVICE/PROCEDURE

The Prolift Pelvic Floor Repair Systems were marketed to physicians beginning in 2005 (even though FDA clearance was not obtained until three years later). These "kits" (anterior, posterior, and total) all contained a pre-cut piece of polypropylene mesh specific to the compartment (Gynemesh PS), the trocars/instruments necessary to insert the mesh devices, a Prolift Surgical Guide, and Instructions for Use. Prolift Anterior was designed to treat a cystocele; Prolift Posterior was designed to treat rectocele; and Prolift Total was designed to treat cystocele, rectocele, and vaginal vault prolapse. Gynemesh PS (cleared in 2002) is the same mesh as Prolene PS mesh, which was cleared by Ethicon in 2000 for the treatment of abdominal wall hernias. Ethicon marketed Gynemesh to urologists, gynecologists, and urogynecologists as "uniquely" designed to treat pelvic organ prolapse, even though there were no studies to support this claim.[1]



Whereas Prolene PS was designed for hernia repairs, Gynemesh PS and Prolift meshes were specifically designed to be used for "vaginal tissue reinforcement and long-lasting

[1] See e.g., ETH.MESH.02280771; ETH.MESH.01156032; ETH-07152; ETH-00252: ("Technologically Advanced by Design – Driven by Innovation"; ETH-00253: "Unique Permanent Material for Durable Solutions"; ETH-00382 ("innovative"; ETH-00384 "Evolution in design for pelvic floor restoration").

stabilization of fascial structures of the pelvic floor in vaginal wall prolapse."[2] According to internal documents, in as early as 1998, Ethicon knew that Gynemesh was not an appropriate mesh for use in the surgical treatment of pelvic organ prolapse, but persisted in launching Gynemesh for prolapse surgery for these reasons: "to raise awareness of the possibility of using a mesh for prolapse repair; to gain entry into this growing market before competitors; to spend time seeking out key surgeons as product champions and to allow time to carry out further market research into what the ideal product for this indication might be."[3]

The Instructions for Use state, "Gynemesh PS elicits a minimum to slight inflammatory reaction, which is transient and is followed by the deposition of a thin fibrous layer of tissue which can grow through the interstices of the mesh, thus incorporating the mesh into adjacent tissue. The mesh remains soft and pliable, and normal wound healing is not noticeably impaired. The material is not absorbed, nor is it subject to degradation or weakening by the action of tissue enzymes."[4] There is ample evidence in the scientific literature, Ethicon corporate documents, and Ethicon employee depositions that this statement is inaccurate – even at the time of the introduction of Prolift. Despite literature to the contrary and confirmatory internal corporate knowledge, Ethicon never changed the IFU to reflect: 1) the inflammatory response is persistent and not transient; 2) the mesh creates dense scar tissue not a "thin layer of tissue"; and 3) the material is, in fact, subject to degradation.[5]

The pre-cut mesh pieces and the instruments contained in the "kit" dictate the procedure. The Prolift operation is a radical departure from any other traditional prolapse repair.[6] It is a complex and difficult procedure to perform with little margin of error when it comes to proper placement. Even Altman[7] and colleagues conclude: "The longer duration of surgery, more frequent use of intraoperative cystoscopy, and greater frequency of bladder perforations and pelvic hemorrhage associated with mesh repair in our study are consistent with the more invasive nature of this procedure as compared with colporrhaphy." It is "not minimally invasive" as claimed by Ethicon in its promotional materials.[8]

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[2] ETH.MESH.01154032.

[3] ETH. MESH.12009028.

[4] See e.g., ETH.MESH.02341522; ETH.MESH.00015690; ETH.MESH.02341454.

[5] ETH.MESH.02341522; ETH.MESH.02341454; ETH.MESH.02001398.

[6] See e.g., ETH.MESH.02282833 ("The TVM represents a MAJOR mind shift on several key aspects of prolapse surgery that may require a greater shift in thinking: … Passage THROUGH the sacrospinal ligaments: -- All of these are new concepts and will require good back up during the education process to explain why they are essential to good results.").

[7] Altman, et al., Anterior Colporrhaphy versus Transvaginal Mesh for Pelvic-Organ Prolapse. N Engl J Med 2011; 364:1826-36.

[8] See e.g., ETH.MESH.03905968.

According to the surgical instructions for use provided by Ethicon, "It is preferred to leave Halban's fascia (pubocervical fascia) on the vaginal wall."[9] This technique places the mesh directly in contact with the bladder wall. It is well documented that the polypropylene mesh incites an inflammatory reaction and, ultimately tissue ingrowth. This technique, recommended by Ethicon, unnecessarily places the bladder at risk for erosion, fistula, scar formation and the development of de novo overactive bladder. In addition, it enhances the likelihood of the mesh becoming incorporated into the bladder wall.

IV. DISCUSSION OF OPINIONS

Transvaginally-placed mesh kits, such as the Prolift devices, cause serious and life-style altering complications including chronic pelvic pain, dyspareunia, nerve injuries, fistulas, urethral obstruction, bladder stones, and vaginal, urethral, and bladder erosion. This opinion is based not only on my own firsthand experience with hundreds of such complications, but also the knowledge gained by speaking to my peers. I have personally operated on over 100 patients with severe synthetic mesh complications, but I have taken care of hundreds more who either did not elect further surgery with me or who simply gave up and were seeking relief from pain management experts.[10] Many patients require multiple operations.

A permanent implantable device, such as the Prolift devices, should not have been designed for placement in a surgically contaminated field, at least without proper animal and clinical studies to document safety and without a clear warning about the possibility of short and long term complications.[11] Bacteria attaches to mesh during the insertion process.[12] Infection, even if

[9] ETH.MESH.00419571.

[10] Deng, et al., (2007). Presentation and management of major complications of midurethral slings: Are complications under-reported? Neurourol Urodyn, 26(1), 46-52.; Reynolds, et al. (2012). Obturator foramen dissection for excision of symptomatic transobturator mesh. J Urol, 187(5), 1680-1684.; Blaivas, J. G. & Chaikin, D. C. (2011). Pubovaginal fascial sling for the treatment of all types of stress urinary incontinence: surgical technique and longterm outcome. Urol Clin North Am, 38(1), 7-15.; Ogah, J., et al. (2011). Minimally invasive synthetic suburethral sling operations for stress urinary incontinence in women: a short version Cochrane review. Neurourol Urodyn, 30(3), 284-291.; Kobashi, K. C., et al., (1999). Erosion of woven polyester pubovaginal sling. J Urol, 162(6), 2070-2072.; FDA Executive Summary." Web; Anger, J. T., et al. (2007). Complications of sling surgery among female Medicare beneficiaries. Obstet Gynecol, 109(3), 707-714.

[11] Culligan, P., et al. (2003). Bacterial colony counts during vaginal surgery. Infect Dis Obstet Gynecol, 11(3), 161-165.; Vollebregt, A., et al. (2009). Bacterial colonisation of collagen-coated polypropylene vaginal mesh: are additional intraoperative sterility procedures useful? Int Urogynecol J Pelvic Floor Dysfunct, 20(11), 1345-1351.; Choi, J. J., et al. (2012). Use of mesh during ventral hernia repair in clean contaminated and contaminated cases: outcomes of 33,832 cases. Ann Surg, 255(1), 176-180.

[12] See e.g., Vollebregt, et al. (2009): Mahmoud, W. M., et al. (1993). Migration of bacteria along synthetic polymeric fibers. Journal Of Biomaterials Science. Polymer Edition, 4(6), 567-578; Klinge, U.,

subclinical, can result in chronic inflammation, scarring, pain, and functional bladder and bowel problems.

Nolfi et al. published a study in the American Journal of Obstetrics and Gynecology entitled "Host Response to Synthetic Mesh in Women with Mesh Complications." In that study, the authors examined the explanted vaginal tissue of 27 women who had received either a polypropylene midurethral sling or a polypropylene prolapse mesh. The authors concluded that a "persistent foreign body response was observed in mesh tissue complexes excised from women requiring surgical excision of mesh months to years after mesh implantation." The authors also concluded that "[i]mportantly, the presence of macrophages was limited to the area immediately surrounding the mesh fibers with each fiber eliciting an independent reaction, the magnitude of which appeared to be proportional to the number of fibers in a given area. This points to the importance of maintaining meshes in a flat (as opposed to folded) configuration to minimize the amount of material per area and choosing meshes in which the spaces between fibers (pores) are wide enough that the host response to two adjacent fibers does not overlap." Notably, the authors also stated that the "Gynemesh PS has a highly unstable geometry when loaded resulting in pore collapse and increasing stiffness of the product mesh deformation (contraction, retraction, or shrinkage) is also frequently observed in meshes removed for pain." The authors also concluded that the "increase in MMP-9 in mesh explants that were removed for exposure indicates degradation; the positive association between interleukin-10 and M2 macrophages in mesh explants that are removed for pain in consistent with fibrosis."

The arms of the Prolift devices create specific problems. These are inserted blindly with trocars through densely vascularized and innervated areas. The edges are sharp and can saw through delicate tissues.[13] There is no such thing as a "tension-free" insertion. These arms undergo stress and stretching at the time of insertion and afterwards as the body reacts to the foreign body. This results in curling, roping, and coiling.[14] Tissue injury can occur at the time of placement or subsequently as the mesh deforms and contracts.

Even though the surgeon may feel that the mesh implant is lying flat at the time of implantation, the mesh is prone to shrink unpredictably and asymmetrically, influenced by

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Klosterhalfen, B., et al. (1998). Shrinking of polypropylene mesh in vivo: an experimental study in dogs. Eur J Surg, 164(12), 965-969.

[13] ETH.MESH.03904451.

[14] ETH.MESH.00034875, email 11-20-2008 from Jonathan Meek to Catherine Lepley and others: "Another point is that the tight-knit arms would result in a rope effect. Knowing that the tissue needs to grow through the arms as-well, this will be problematic in the patient. To be fair, it is an issue for everyone because if you 'yank' Gynemesh arms, they will also lose their porosity. The effect of roping is increased inflammatory response, increased risk of infection and denser scar plate (not much fun for the patient) …"; ETH-80647.; Kirkemo dep. (4-18), at p.135-138, p.150; Hinoul dep. (4-6), p.506-507.

individual response, bacterial contamination, anatomical location, and time.[15] Mesh deforms *in vivo*. Retraction, shrinkage, banding, bunching, and folding lead to pain and contracture.

There is evidence that polypropylene mesh degrades *in vivo*[16] and that degradation results in stiffening of the mesh, perpetuation of the inflammatory response, creation of a nidus for bacteria and other organisms, and the production of unknown and potentially toxic and/or carcinogenic chemicals. The breakdown of mesh is expected to result in the presence of small molecular complexes and chemical products of degradation, as is the case for any polymerized hydrocarbon. Accumulations of polypropylene degradation products are expected to be confined within the scar capsule and have more local, rather than systemic, effects on the body, owing to their fibrous encapsulation; however, no published studies currently address this point. The degradation products might act as an additional stimulus for the chronic inflammatory response. Accumulation and toxicity of these degradation products might cause tissue damage and contribute to the continuous remodeling around the mesh filaments and extension of fibrosis.[17] I recently published a review article in *Nature*.[18] Although this article dealt primarily with slings, the discussion of the material properties of polypropylene mesh when used in the vagina and the

[15] See e.g., Mesh shrinkage: How to assess, how to prevent, how to manage? PowerPoint ("Mesh Shrinkage . . . Is real! . . . May result in unpredictable way in severe complications including dyspareunia, pain and recurrence."); Mamy, L., et al. (2011). Correlation between shrinkage and infection of implanted synthetic meshes using an animal model of mesh infection. Int Urogynecol J, 22(1), 47-52. ; Letouzey, V., et al. (2012). Is polypropylene mesh coated with antibiotics is efficient to prevent mesh infection and contraction in an animal infectious model? [Abstract]. 37th Annual Meeting of the International Urogynecological Association, 193; Jacquetin, B., & Cosson, M. (2009). Complications of vaginal mesh: our experience. Int Urogynecol J Pelvic Floor Dysfunct, 20(8), 893-896.; Feiner, B., & Maher, C. (2010). Vaginal mesh contraction: definition, clinical presentation, and management. Obstet Gynecol, 115(2 Pt 1), 325-330.; Tunn, R., et al. (2007). Sonomorphological evaluation of polypropylene mesh implants after vaginal mesh repair in women with cystocele or rectocele. Ultrasound Obstet Gynecol, 29(4), 449-452.

[16] Iakovlev VV, et al. *Degradation of polypropylene in vivo: A microscopic analysis of meshes explanted form patients.* J Biomed Mater Res B Appl Biomater. 2015 Aug 28. doi: 10.1002/jbm.b.33502. [Epub ahead of print].; Jongebloed, W. L. & Worst, J. F. (1986). Degradation of polypropylene in the human eye: a SEM-study. Documenta Ophthalmologica. Advances In Ophthalmology, 64(1), 143-152.; Coda, A., et al. (2003). Structural alterations of prosthetic meshes in humans. Hernia: The Journal Of Hernias And Abdominal Wall Surgery, 7(1), 29-34.; Costello, C. R., et al. (2007). Materials characterization of explanted polypropylene hernia meshes. Journal of Biomedical Materials Research Part B: Applied Biomaterials, 83B(1), 44-49.; Clavé, A., et al. (2010). Polypropylene as a reinforcement in pelvic surgery is not inert: comparative analysis of 100 explants. Int Urogynecol J, 21(3), 261-270.; Sternschuss, G. (2012). Post-Implantation Alterations of Polypropylene in the Human. J Urol. 188 (7), 27-32.

[17] Junge, K. et al. Persistent extracellular matrix remodelling at the interface to polymers used for hernia repair. Eur. Surg. Res. 35, 497–504 (2003).

[18] Blaivas, J. G. et al., Safety considerations for synthetic sling surgery. Nat Rev Urol. 2015 Sep;12(9):481-509. (Epub 2015 Aug 18).

body's responses are the same as those seen with prolapse devices. These properties are well reported elsewhere and, based on my review of corporate documents, known to Ethicon.[19]

Degradation was reported in papers by Iakovlev et. al and Imel et. al on the in vivo degradation of transvaginally implanted polypropylene products. Degradation progresses over time and results in clinically significant embrittlement, loss of flexibility, mesh stiffening and deformation.[20,21] Iakovlev, et al. studied 164 excised meshes "to search for features of polypropylene degradation" and concluded that "polypropylene degradation can be detected by readily available conventional light microscopy. A number of features indicated that polypropylene degrades while in the body." Bendavid reported on the mechanism of hernia mesh repair pain. This new clinical syndrome, characterized by slow onset, relentless progression, and uncompromising lack of response to treatment, was attributed to nerve entrapment encased in dense scar tissue. According to the author, the pores of mesh need to be viewed as "mini-compartments" of biological tissue where the vasculature, nerves and their receptors are exposed to potential mechanical and chemical factors: scarring, entrapment, compression, tugging, deformation, contraction, hypoxia/acidosis, inflammation and edema.[22] In another study by Bendavid et. al, a marked increase in nerve density trapped in scar was observed in patients who had mesh-related pain, regardless of the surgical technique or surgical location.[23] Testing by Lee also discussed the mechanisms of chronic pain after MUS surgery, describing a "complex interplay of factors [that] can be causative, including synthetic material type, nerve and muscle injury, infection, contraction, erosion or extrusion."[24]

In an article published in Biomaterials entitled "In vivo oxidative degradation of polypropylene pelvic mesh," the authors found that the "overall degradation process of PP pelvic meshes may be summarized as follows. The implant causes increased activity by oxidative enzymes in the vicinity of the implant. This leads to an oxidative degradation process that is evidenced by appearance of hydroxyl and then carbonyl groups in the polypropylene, as observed by infrared spectra. There is accompanying degradation of the polypropylene molecular weight, and this process may be delayed, but not prevented, by the presence of antioxidants in the

[19] See e.g., ETH.MESH.02589032; Mesh shrinkage: How to assess, how to prevent, how to manage? PowerPoint.

[20] Iakovlev VV, et al. Degradation of polypropylene in vivo: A microscopic analysis of meshes explanted form patients. 2015:00B:000-000, p10.

[21] Imel A, et al. In vivo oxidative degradation of polypropylene pelvic mesh. Biomaterials. 2015 Dec;73:131-41, 132.

[22] Bendavid R, et al. Mesh-related SIN syndrome. A surreptitious irreversible neuralgia and its morphologic background in the etiology of post-herniorrhaphy pain. Int J Clin Med. 2014; 5:799-810, 799.

[23] Bendavid R, et al. A mechanism of mesh-related post-herniorrhaphy neuralgia. Hernia. 2015 Nov 23, p6. [Epub ahead of print].

[24] Lee 2015, 205.

polypropylene. Antioxidants are preferentially consumed by the oxidizing species and finally the concentration falls below a level required to protect the polymer and oxidative degradation occurs. This degradation is accompanied by a decrease in mechanical properties (embrittlement, loss of mass, decreased melting temperature, reduced compliance) of the polypropylene. In particular, the surface and amorphous regions of the polypropylene are selectively degraded, resulting initially in cracks and, on longer exposure, fragmentation of the implant.

Recently published animal studies also support these opinions. The American Journal of Obstetrics and Gynecology published a study entitled "Characterization of the host inflammatory response following implantation of prolapse mesh in rhesus macaque." In that study, the authors concluded that their "findings correlate with those of a previous study demonstrating that lighter-weight, higher-porosity mesh was also associated with fewer negative effects on vaginal tissue quality. This suggests that the chronic M1 pro-inflammatory response to mesh may drive tissue degradation eventually leading to mesh exposures over time similar to what is observed clinically; however, additional work is required to establish a causal relationship."

Ethicon marketed Prolift as a one-size-fits-all technique for prolapse repair that is reproducible.[25] However, the anatomy of prolapse and the relationship between surface landmarks and vital structures varies from individual to individual and even in the same individual, making accurate and safe placement of trocars unpredictable.." For example, positioning of the patient in various degrees of dorsal lithotomy position can impact the locations of nerves and blood vessels. The size of the obturator foramen and the bony pelvis can vary.[26] The Prolift devices pass dangerously close to vital structures.[27] Although bleeding can often be controlled, nerve injuries can have disastrous consequences.

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[25] See e.g., ETH-03430 ("Gynecare's challenge is to enter the market with a product *and* technique that will allow gynecologists, urogynecologists, and urologists to perform a quick, efficient and reproducible procedures for the treatment of these pathologies."); ETH.MESH.00419571, at p. 2 ("The objective of the Prolift procedure is to achieve a complete anatomic repair of pelvic floor defects in a standardized way.").

[26] Whiteside JL, Walters MD. Anatomy of the obturator region: relations to a trans-obturator sling. Urogynecol J Pelvic Floor Dysfunct. 2004 Jul-Aug;15(4):223-6.; LitWiller, J., et al. Effect of Lithotomy Positions on Strain of the Obturator and Lateral Femoral Cutaneous Nerves. Clinical Anatomy 17:45-49 (2004).

[27] Whiteside, JL (2004); Atassi, Z., et al. Haemorrhage and nerve damage as complications of TVT-O procedure: case report and literature review. Arch Gynecol Obstet (2008) 277:161–164.; Marqués Queimadelos A, et al. (2004) Cabestrillo suburetral transobturatriz en el tratamiento de la incontinencia urinary de esfuerzo femenina. Rev Med Univ Navarra 48:62–69.; Hazewinkel, M., et al. Persistent groin pain following a trans-obturator sling procedure for stress urinary incontinence: a diagnostic and therapeutic challenge. Int Urogynecol J (2009) 20:363–365.; Hinoul, P., et al. Anatomical variability in the trajectory of the inside-out transobturator vaginal tape technique (TVT-O). Int Urogynecol J (2007) 18:1201–1206.; Spinosa JP, et al.. Transobturator surgery for female urinary continence: a comparative anatomic study of outside-in vs inside-out techniques. Prog Urol 15(4):700-6, 2005. BJU International 2007 Journal Compilation, 100, 1097-1102.

Claims that make the procedure sound as if it is safer and easier to perform than it actually is are misleading. The goal was sound – a simple, safe, efficacious, outpatient procedure that required minimal surgical skills and could be mastered by surgeons with little training.[28] But the truth is very different. The fact is, it is not so easy to learn these techniques and the ergonomics of the trocars are such that it is easy to misguide them and end up in the wrong place. Because the company so trivialized the learning curve and potential complications, many surgeons with inadequate skill and experience perform these surgeries. In addition, there is ample evidence in the literature that it is very common for the trocars to inadvertently puncture vital structures during trocar passage.[29]

Due to tissue ingrowth, it is very difficult and often impossible to remove the entire mesh and, in most instances, there are remnants of mesh that remain after explant surgery This is well known.[30] The arms of the Prolift devices are implanted in spaces that are not easily accessed and foreign to most urologists and gynecologists. The sheer size and configuration of the Prolift meshes alone make complete removal virtually impossible. Further, these explant surgeries are risky and have their own set of complications. It is impossible to remove the device without also excising heathy tissue. Further, the mesh that remains behind can form the nidus for infections, stones, more erosion, scar formation or extrusion and pain. There are neither published guidelines nor good studies of the outcomes after mesh removal. Consequently explant surgery is mostly empiric and many surgeons opt to do an incomplete operation, subjecting the patient to poor results or further surgery.[31] On the other hand, overzealous surgeons who attempt to remove all the mesh may cause even more problems. In brief, when performing explant surgery, most surgeons simply do not know what is best.

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[28] ETH-60149 ("One of our biggest challenges moving forward will be our ability to clearly communicate with our physicians how to use Gynemesh tension free in POP procedures. This will also help to ensure a healthy pipeline of targets for Prolift moving forward. This information should be helpful in shorten [sic] the learning curve with your physicians that are just starting to use mesh. We need to prepare our future Prolift users, today.").

[29] See e.g., Bhoyrul S, et al. Trocar injuries in laparoscopic surgery. Journal of the American College of Surgeons. 2001;192(6):677-83.; Shindel AW, Klutke CG. Urethral slings placed by the transobturator approach: evolution in the technique and review of the literature. Current Urology Reports. 2005;6(5):385-92.; Takeyama M et al. Nerve preservation in tension-free vaginal mesh procedures for pelvic organ prolapse: a cadaveric study using fresh and fixed cadavers. Int Urogynecol J 2008 Apr; 19(4): 559-566. Epub 2007 Oct 10.; Chen CCG et al. Anatomic relationships of the tension-free vaginal mesh trocars. Am J Obstet Gynecol 2007; 197: 666.e1-666.e6.; Roundtable: Using mesh to repair prolapse: Averting, managing complications. Karram MM, moderator. OBG Management 2009; 21 (2): 21-28.; see e.g.,ETH.MESH.00857821; ETH-02601.

[30] Reynolds, W. S., et al. (2012). Obturator foramen dissection for excision of symptomatic transobturator mesh. J Urol, 187(5), 1680-1684.

[31] Barber M., Surgical Techniques for Removing Problematic Mesh, Clinical Obstetrics and Gynecology, Volume 56, Number 2, 289–302

The management of mesh complications is fraught with complexity and results in a high rate of persistent symptoms. [32] Appropriate and unbiased clinical testing, if performed, would have shown the problems and complications associated with armed pelvic organ prolapse kits, like Ethicon's Prolift. Because of the known complications, many occurring years after the original surgery,[33] it behooved the company to conduct long-term clinical trials or at least monitor complications through a registry. Had they done this Ethicon undoubtedly would have uncovered the complications.

The most debilitating and challenging complication to treat is chronic pain, especially as it is seen with transvaginally-placed mesh for prolapse.[34] This pain can be located in the abdomen, pelvis, vagina, buttocks, perineum, groin, or leg. It can be acute (occurring immediately after surgery) or chronic with an insidious onset. It is often refractory to traditional treatments. It can be related to erosion; scarring; mesh deformation; entrapment or compression of large nerves with classic or atypical nerve distribution; entrapment of smaller nerve branches with diffuse distribution; muscular inflammation, scarring, trauma, and hypertonicity; or visceral pain syndromes. It may be associated with other sensory changes such as numbness and tingling. It may continue, or even worsen, after mesh excision or revision.[35] New treatment modalities for pelvic

[32] See e.g., Barski D and Deng DY. Management of mesh complications after SUI and POP repair: Review and analysis of the current literature. Biomed Res Int. 2015;2015:831285. [Epub 2015 Apr 20].; Lee D, et al. Meshology: a fast-growing field involving mesh and/or tape removal procedures and their outcomes. Expert Rev Med Devices. 2015 Mar;12(2):201-16; Dunn, et al., Changed Women: The Long-Term Impact of Vaginal Mesh Complications. Female Pelvic Med Reconstr Surg 2014;20: 131Y136.; Unger, C., et al. Outcomes following treatment for pelvic floor mesh complications. Int Urogynecol J. 2014 Jun;25(6):745-9.; Skala, CE, et al. Mesh complications following prolapse surgery: management and outcome. Eur. J Obstet. Gynecol. 159 (2011) 453-456.; Nguyen, JN, et al. Perioperative Complications and Reoperations after Incontinence and Prolapse Surgeries Using Prosthetic Implants. Obstet Gynecol 2012;119:539–46; Huffaker, et al. A serious complication following placement of posterior Prolift, Int Urogynecol J (2009) 20:1383–1385; Brubaker and Shull, A perfect storm, In t Urogynecol J (2012) 23:3-4; Hurtado, E. and Appell, R. Management of complications arising from transvaginal mesh kit procedures: a tertiary referral center's experience. Int Urogynecol J (2009) 20:11–17.

[33] See e.g., Hansen, B, et al. Long-Term Follow-up of Treatment for Synthetic Mesh Complications. Female Pelvic Med Reconstr Surg. 2014 May-Jun;20(3):126-30.

[34] Rogo-Gupta, L. and Raz, S. Pain Complications of Mesh Surgery. H.B. Goldman (ed.), Complications of Female Incontinence and Pelvic Reconstructive Surgery, 87 Current Clinical Urology.; Bako, A. and Dhar, R. Review of synthetic mesh-related complications in pelvic floor reconstructive surgery. Int Urogynecol J (2009) 20:103–111; Lin, LL, et al. Dyspareunia and chronic pelvic pain after polypropylene mesh augmentation for transvaginal repair of anterior vaginal wall prolapse. Int Urogynecol J (2007) 18:675–678.

[35] Crosby, EC, et al. Symptom Resolution After Operative Management of Complications From Transvaginal Mesh. Obstet Gynecol 2014;123:134–9.; Lee, D., et al. Transvaginal Mesh Kits—How "Serious" Are the Complications and Are They Reversible? UROLOGY 81: 43e49, 2013.; Margulies, RU, et al. Complications requiring reoperation following vaginal mesh kit procedures for prolapse. Am J Obstet Gynecol 2008;199:678.e1-678.e4.; Unger, C., et al. Outcomes following treatment for pelvic floor mesh complications. Int Urogynecol J. 2014 Jun;25(6):745-9.

pain have been developed as a response to this pain management challenge, rarely used in urology or gynecology until the appearance of mesh-related pain. These include trigger point injections, nerve blocks, Botox injection, physical therapy, treatment with medications for chronic, neuropathic pain, and referral to contract-based pain management programs.[36]

The complications discussed in this report and in the medical literature are a result of the defects in the device itself. Complications may occur even in experienced hands and when proper surgical technique is used.[37] Ethicon's marketing materials suggest that these complications occur mostly because of faulty surgical technique performed by inexperienced or poorly trained surgeons, perhaps by "over-tensioning" or misplacement. However, I have firsthand knowledge that is not the case. In the course of my practice, I have seen mesh complications from many world renowned experts and, from discussions with my colleagues, I know of many others. The peer-reviewed literature also supports this concept.[38]

Mesh complications are significantly under-reported.[39] Additionally, most patients who experience complications do not return to their original surgeons, contributing to a misperception among individual physicians that their outcomes are better than they, in fact, are.[40]

I have reviewed the Instructions for Use for the Prolift devices. Ethicon did not warn doctors and patients about the chronic and lifestyle altering nature of the complications associated with its products which included chronic and debilitating pain, dyspareunia, sexual impairment, nerve injuries, vaginal scarring, bladder dysfunction, new onset stress urinary incontinence, severe bladder and bowel dysfunction, the need for multiple corrective surgeries, and others.[41] Because

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[36] See e.g., Gyang,AN, et al. Managing chronic pelvic pain following reconstructive pelvic surgery with transvaginal mesh. Int Urogynecol J (2014) 25:313–318.

[37] See e.g., Iglesia CB, et al. Vaginal mesh for prolapse: a randomized controlled trial [reply]. Obstet Gynecol 2010; 116: 1457 ("If expert surgeons from multiple institutions cannot get the outcomes of a few individuals, perhaps there is something wrong with the procedure").

[38] Jacquetin, B, et al. Total transvaginal mesh (TVM) technique for treatment of pelvic organ prolapse: a 3-year prospective follow-up study. Int Urogynecol J (2010) 21:1455–1462.

[39] See e.g., Deng, D. Y., et al. (2007). Presentation and management of major complications of midurethral slings: Are complications under-reported? 1Neurourol Urodyn. 2007;26(1):46-52.; Anger, J. T., et al. (2007). Complications of sling surgery among female Medicare beneficiaries. Obstet Gynecol, 109(3), 707-714.

[40] Blandon, R., et al. (2009). Complications from vaginally placed mesh in pelvic reconstructive surgery. Int Urogynecol J 20, 523-531.; Rostaminia, G., Shobeiri, A., et al. Referral pattern for vaginal mesh and graft complications to the University of Oklahoma Pelvic and Bladder Health Clinic. J Okla State Med Assoc. 2012; 105(9):356-8.; Ostergard, D. Lessons from the past: directions for the future. Int Urogynecol J (2007) 18:591-598.

[41] ETH.MESH.02341522; ETH.MESH.02341454; ETH.MESH.02001398; see e.g., ETH-03558; ETH.MESH.00267981 at 00237992; ETH-08343 (erosion and abscess formation); ETH-10127; ETH-

the company so trivialized the learning curve and potential complications, many surgeons with inadequate skill and experience perform these surgeries. Ethicon did not warn doctors and patients about the difficulty removing their Prolift products and the poor or less than optimal results when excision or revision becomes warranted due to complications. Ethicon did not attempt to establish best practices for management of complications.[42]

I have reviewed the Material Safety Data Sheet for the polypropylene used in the Prolift medical devices.[43] This document, under INCOMPATIBILITY, states that the following materials are incompatible with this product: "Strong oxidizers such as chlorine, peroxides, chromates, nitric acid, perchlorates, concentrated oxygen, sodium hypochlorite, calcium hypochlorite and permanganates. Chlorine; Nitric acid." And yet, many of these chemicals are routinely found in human tissue. The document also states under COMPONENT TOXICITY: "Polypropylene has been tested in laboratory rats by subcutaneous implantation of discs or powder. Local sarcomas were induced at the site of implantation." Ethicon IFUs do not include the toxic and carcinogenic warnings contained in the MSDSs. Ethicon marketing materials for doctors and patients do not include the toxic and carcinogenic warnings contained in the MSDSs.[44]

Questions have been raised in the peer-review literature regarding the carcinogenic potential for transvaginally placed polypropylene mesh. We addressed this concern in our Nature review. These carcinogenic effects, leading to the development of sarcomas, have been studied in animal models. The basic research and clinical data suggest that implantation of polypropylene mesh might increase the risk of sarcoma. If a risk is present in humans, it is likely to be very low. Mutagenic effects, in general can take many years to accumulate and then a long period to cause a neoplasm. Detecting any oncogenic effects of SMUS implants would require a large cohort of patients with the same type of implant, and these patients would have to be followed up for a sufficiently long period of time, most likely at least 15 years.[45] However, a recent case of clear cell carcinoma associated with an eroded polypropylene sling was reported November, 2015 in the International

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08926 (pain); ETH-08894; ETH-08776; ETH-00639; ETH-09541 (erosion, fistula, pain); see also, ETH.MESH.00164023. See e.g., Zhang, L, et al. Postoperative voiding difficulty and mesh-related complications after Total Prolift System surgical repair for pelvic organ prolapse and predisposing factors. Menopause. 2015 Aug;22(8):885-92.

[42] Blaivas, J. G., et al. (2013). Salvage Surgery after Failed Treatment of Synthetic Mesh Sling Complications. J Urol. 2013 Oct;190(4):1281-6.; Unger, C., Abbot, S., Evans, J., Jallad, K., Mishra, K., Karram, M., Iglesia, C., Rardin, C., Barber, M. Outcomes following treatment for pelvic floor mesh complications. Int Urogynecol J. 2014 Jun;25(6):745-9.

[43] Sunoco 2004 MSDS; Sunoco 2006 MSDS; Sunoco 2005 MSDS.

[44] ETH.MESH.02341522;ETH.MESH.02341454;ETH.MESH.02001398;ETH.MESH.03905968; ETH.MESH.03905976; ETH.MESH.03905992; ETH.MESH.03906001; ETH.MESH.03906037.

[45] Blaivas 2015, 481-509, 500.

Urogynecology Journal.[46] A second case of squamous cell carcinoma associated with a midurethral sling was reported at the same time. In an accompanying editorial in the same journal issue, Goldman recognized that a cause-and-effect pattern could be concerning and recommended vigilance.[47] This is new information that supports my opinions that patients who receive mesh products should be monitored closely over a long-term period.

I have reviewed the literature regarding the safety and efficacy of Prolift, as well as the literature regarding mesh kits for the repair of prolapse generally. In my opinion, the medical literature does not support the conclusion that the Prolift devices are safe and there a number of studies that call into question its efficacy. Summaries of some of the more important studies are included in this report.

In 2010, Jacquetin[48] reported on the 3-year results of a study French TVM. At 1-year follow-up, recurrent prolapse was reported in 17.4% of patients; at 3-years, 20% had failed. Over the three year period, 33.3% of patients had reoperations for recurrence, complications (exposure, vesicovaginal fistula, hematoma), and stress urinary incontinence. Moderate or severe vaginal stiffness (loss of elasticity) could be detected by digital examination in 11 (12.6%) patients after 1 year. Of the 61 patients who were sexually active at baseline, only 36 (59%) remained so at 3 year.

Velemir[49] also reported on the French TVM study (2010), looking at mesh retraction. Patients with no, moderate (<50%) or severe (≥50%) mesh retraction were compared. Mesh retraction, also known as mesh shrinkage or contraction, was defined, in this study, as a reduction of the surface area of the original implanted mesh. Velemir found that anterior mesh retraction was moderate in 80% and severe in 9.3% in the patients studied. Posterior mesh retraction was moderate in 48.4% and severe in 9.7% of patients. With both anterior and posterior Prolift mesh implants, mesh retraction was strongly associated with increased mesh thickness and higher frequency of recurrent prolapse. The authors also concluded that "over time it appeared that mesh retraction was probably a contributing factor to recurrence, postoperative pain and dyspareunia."

The U.S. TVM study, reported in 2011 by Miller,[50] provided 5-year results. The overall failure rate was 33.3% at 5 years. The authors inaccurately used the total study population as the

[46] Lin HZ, et al. A first reported case of clear cell carcinoma associated with delayed extrusion of midurethral tape. Int Urogynecol J. 2015 Nov 20. [Epub ahead of print].

[47] Goldman HB and Dwyer. Polypropylene mesh slings and cancer: An incidental finding or association? Int Urogynecol J. 2015 Nov 19, p2. [Epub ahead of print].

[48] Jacquetin, B, et al. Total transvaginal mesh (TVM) technique for treatment of pelvic organ prolapse: a 3-year prospective follow-up study. Int Urogynecol J (2010) 21:1455–1462.

[49] Velemir, L., Transvaginal mesh repair of anterior and posterior vaginal wall prolapse: a clinical and ultrasonographic study. Ultrasound Obstet Gynecol 2010; 35: 474–480.

[50] Miller, D., et al. Prospective Clinical Assessment of the Transvaginal Mesh Technique for Treatment of Pelvic Organ ProlapseV5-Year Results. Female Pelvic Med Reconstr Surg 2011;17: 139-143.

denominator for calculating complications rather than the number of patients who participated in the 5 year evaluation. The true mesh exposure rate was 24% and voiding dysfunction rate 9%. A total of 44% (29 of 66 women) required reoperation, including 13 for stress incontinence, at least 9 for mesh exposure, 5 for recurrent prolapse, and 2 for fistulas. Similar to the French TVM study, nearly one-third of preoperatively sexually active women abandoned sexual activity after the Prolift procedure,

A randomized controlled trial of Prolift vs. traditional anterior colporrhaphy was begun in 2007 and reported in 2010 [51]. The trial was halted early because of an unacceptably high rate of vaginal erosion (15.6%). Sokol[52] reported 1-year results on the same cohort of patients. At 12 months, both groups had improvement of pelvic organ prolapse, but mesh repairs had higher reoperation rates. The authors concluded: Nonetheless, properly designed clinical trials are necessary to evaluate whether synthetic mesh confers benefit for vaginal prolapse repair. Based on the results of this study and the high exposure rates that have been noted in other studies, it is very likely that the risks outweigh the benefits for the older trocar-based mesh systems, even when fellowship-trained pelvic reconstructive surgeons perform these procedures.

Altman[53] published the results of a randomized controlled study with Prolift Anterior and anterior colporrhaphy. The mesh repair group, as compared with the anterior colporrhaphy group, had a significantly longer mean duration of surgery, greater mean intraoperative blood loss, more frequent need for intraoperative cystoscopy, and more bladder perforations. The mesh group also had higher rates of new onset stress urinary incontinence. As compared with anterior colporrhaphy, use of a standardized, trocar-guided mesh kit for cystocele repair resulted in higher short-term rates of successful treatment, according to the authors, but also in higher rates of surgical complications and postoperative adverse events.

Withagen published two articles reporting on the same study population, a randomized controlled trial of Prolift anterior vs. traditional non-mesh repair. All patients in the study had recurrent prolapse. At one year,[54] anatomic outcomes were better in the Prolift group, but subjective improvement occurred in equal proportions in both groups (80% in Prolift and 81% non-mesh). Intraoperative and postoperative complications were more frequent in the Prolift group. In the Prolift group, 16.9% developed mesh exposure. The authors recognized that "the effects of long-term presence of non-absorbable mesh in the vagina is unknown and a reason for concern." Because the long-term effects and safety of mesh-reinforced repairs are not yet fully

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[51] Iglesia, C., et al. Vaginal Mesh for Prolapse, A Randomized Controlled Trial. Obstet Gynecol 2010;116:293–303.

[52] Sokol, AI, et al. One-year objective and functional outcomes of a randomized clinical trial of vaginal mesh for prolapse. Am J Obstet Gynecol 2012;206:86.el-9.

[53] Altman, et al., Anterior Colporrhaphy versus Transvaginal Mesh for Pelvic-Organ Prolapse. N Engl J Med 2011; 364:1826-36.

[54] Withagen, MI, et al. Trocar-Guided Mesh Compared With Conventional Vaginal Repair in Recurrent Prolapse. Obstet Gynecol 2011;117:242-50.

known, surgeons may consider these procedures primarily for recurrent vaginal prolapse after counseling patients on the risks and benefits. In the second article (2012),[55] Withagen reported a much higher frequency of new prolapse in untreated compartments in the Prolift group. At 1 year after surgery, 10 of 59 women (17%) in the non-mesh group versus 29 of 62 women (47%) in the Prolift group were diagnosed with new prolapse stage II or higher in the untreated compartment.

These articles are consistent with my experience. Improved anatomic results are misleading and likely the result of stiffening and loss of compliance in the vaginal wall. Complications are greater in mesh repairs and reoperations higher. New onset stress urinary incontinence and prolapse in a non-mesh compartment occur frequently and are also a result of the non-anatomical correction provided with the Prolift devices.

Mesh complications are also significantly under-reported.[56] In addition, most patients who experience complications do not return to their original surgeons, contributing to a misperception among individual physicians that their outcomes are better than they, in fact, are.[57] Even though the medical literature for transvaginally-placed prolapse mesh is flawed for reasons including, but not limited to, industry sponsorship, bias, industry manipulation of data, inappropriate choice of outcome variables, and lack of long-term follow-up, the results are not good.

Regarding **efficacy of mesh kits**, I agree with the conclusions that the FDA made from their own literature review: "The literature review found that while transvaginal POP repair with mesh often restores anatomy, it has not been shown to improve clinical benefit over traditional non-mesh repair."[58]

- Although there was some early evidence of anatomic improvement with repair using mesh in the anterior compartment, there is little evidence that POP repair surgery with mesh results in any better outcomes in terms of relief of symptoms and QOL measures, which ultimately are the clinically significant indicators for measuring treatment success for this condition.

[55] Withagen, MI, Development of de novo prolapse in untreated vaginal compartments after prolapse repair with and without mesh: a secondary analysis of a randomised controlled trial. BJOG 2012;119:354–360.

[56] See e.g., Deng, D. Y., et al. (2007). Presentation and management of major complications of midurethral slings: Are complications under-reported? Neurourol Urodyn, 26(1).; Anger, J. T., et al. (2007). Complications of sling surgery among female Medicare beneficiaries. Obstet Gynecol, 109(3).

[57] Blandon, R., et al. (2009).Complications from vaginally placed mesh in pelvic reconstructive surgery. Int Urogynecol J 20, 523-531.; Parnell, B., Johnson, E., & Zolnoun, D. Genitofemoral and Perineal Neuralgia After Transobturator Midurethral Sling. Obstet Gynecol (2012;119) 428–431.; Rostaminia, G., Shobeiri, A., et al. Referral pattern for vaginal mesh and graft complications to the University of Oklahoma Pelvic and Bladder Health Clinic. J Okla State Med Assoc. 2012; 105(9):356-8.; Ostergard, D. Lessons from the past: directions for the future. Int Urogynecol J (2007) 18:591-598.

[58] FDA, Urogynecologic Surgical Mesh: Update on the Safety and Effectiveness of Transvaginal Placement for Pelvic Organ Prolapse (July 2011).

- There is no convincing evidence that transvaginal apical or posterior wall repair with mesh results in a better anatomic outcome than repair without mesh.

- Most of the recurrences of prolapse following transvaginal surgery, with or without mesh placement, are at a low stage, are asymptomatic, and do not require further intervention.

- To date, no study comparing transvaginal surgery for anterior wall prolapse with surgical mesh placement to surgery without mesh has demonstrated convincingly a clinically significant difference in terms of subjective success, QOL outcomes, and reoperation for prolapse or incontinence.

- Mesh repairs invariably have a higher rate of reoperations when recurrent prolapse and complications are considered.

Although mesh kits were marketed based on perceived high failure rates with native tissue repairs, a great deal of literature contradicts any claims that prolapse mesh kits improve efficacy outcomes. In the Weber study[59] originally published in 2001 and reanalyzed by Chmielewski[60] in 2011, repairs with polyglactin 910 mesh (absorbable) offered no advantage over traditional repairs regarding efficacy. The authors found no statistically or clinically significant differences between the groups in (a) the rate of prolapse beyond hymen, (b) the absence of pelvic organ prolapse symptoms, (c) reoperations for POP, and (d) all three outcomes combined. Stanford reviewed the literature on the success of native tissue anterior repairs compared to mesh-augmented repairs and found the success rates to be similar. Oversand[61] concluded that native tissue repairs for prolapse should be the first choice in treating primary POP because of low reoperation rates with excellent subjective and objective results and few complications. Funk and Visco[62] analyzed 27,809 prolapse surgeries from an insurance database and found that vaginal mesh and native tissue repair for anterior prolapse had similar 5-year risks for recurrent prolapse. The authors also determined that anterior vaginal wall prolapse was associated with an increased risk of any repeat surgery, which was driven by surgery for mesh removal

Regarding safety of mesh kits, there is a great deal of literature documenting the lifestyle-altering complications that occur with mesh repairs, including erosion, chronic pain syndromes,

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[59] Weber, AM, et al. Anterior colporrhaphy: A randomized trial of three surgical techniques. Am J Obstet Gynecol. 2001 Dec;185(6):1299-304.

[60] Chmielewski, L., et al. Reanalysis of a randomized trial of 3 techniques of anterior colporrhaphy using clinically relevant definitions of success. Am J Obstet Gynecol 2011;205:69.e1-8.

[61] Oversand, SH, et al. Long-term follow-up after native tissue repair for pelvic organ prolapse. Int Urogynecol J. 2014 Jan;25(1):81-9.

[62] Funk, MJ, et al. Long-term outcomes of vaginalmesh versus native tissue repair for anterior vaginal wall prolapse. Int Urogynecol J (2013) 24:1279–1285.

shrinkage and contraction causing vaginal shortening, tightening, and vaginal pain, infections, new onset stress urinary incontinence, and bladder and bowel dysfunction.

We are now seeing reports in the medical literature on large series of serious complications associated with vaginal mesh. For example, over a thousand patients with complications so severe as to require mesh removal surgery are described in these publications in recent years, written by surgeons usually in academic medical centers who are having to "clean up the mess". These articles are coming from surgeons who perform these difficult mesh explant surgeries – often termed "salvage surgeries". One such article termed this new field of medical practice, "Meshology".[63] Another, Crosby (2014)[64] at the University of Michigan reported on 90 patients who received vaginal mesh and underwent removal surgery. The most common presenting signs and symptoms were: pelvic or vaginal pain, 64%; mesh exposure, 62%; a bulge sensation, 30%; and dyspareunia, 48% with most patients reporting more than one symptom. The authors found that only 51% of patients had complete resolution of all symptoms and pain was only treated successfully in 51% of patients. I reported a series of "salvage surgery" [65] following sling complications, also finding that sling removal surgery could be successful, but often required multiple surgeries. In my series, only 28% of women with pain as the presenting complaint considered the surgery a success. Hansen (2014)[66] at the University of Utah, reported a series of 111 women who were evaluated for complications associated with synthetic vaginal mesh. The most common complications were extrusion (65%), contraction (17%), and chronic pelvic pain (16%). The authors found that, despite their best efforts, two years after treatment (4.5 years after the index mesh surgery), women continued to report symptoms that negatively impacted their quality of life. These authors also found that the number of patients presenting with mesh complications increased every year of the study. In the companion article by Dunn (2014),[67] titled "Changed Women: The Long-Term Impact of Vaginal Mesh Complications," the authors described the physical and emotional pain caused by mesh complications, including the feeling of hopelessness when they were informed that "there was nothing else we could do."

Finally, Ethicon colluded with American Medical Systems, Inc. (AMS), C.R. Bard, Inc., and Boston Scientific Corporation (BSC) to influence reimbursement for mesh procedures, knowing that higher payments would increase usage of mesh products by hospitals and doctors.

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[63] Lee D, et al. Meshology: a fast-growing field involving mesh and/or tape removal procedures and their outcomes. Expert Rev Med Devices. 2015 Mar;12(2):201-16.

[64] Crosby, EC, et al. Symptom Resolution After Operative Management of Complications From Transvaginal Mesh. Obstet Gynecol 2014;123:134–9.

[65] Blaivas, J. G., et al. (2013). Salvage Surgery after Failed Treatment of Synthetic Mesh Sling Complications. J Urol. 2013 Oct;190(4):1281-6..

[66] Hansen, B, et al. Long-Term Follow-up of Treatment for Synthetic Mesh Complications. Female Pelvic Med Reconstr Surg. 2014 May-Jun;20(3):126-30.

[67] Dunn, et al., Changed Women: The Long-Term Impact of Vaginal Mesh Complications. Female Pelvic Med Reconstr Surg 2014;20: 131Y136.

Ethicon participated in the formation of the Pelvic Health Coalition (PHC). The PHC consisted of a group of pro-mesh doctors selected by mesh manufacturers to influence reimbursement for mesh procedures.

The address of the PHC is the Washington, DC office of the Reed Smith law firm. I reviewed public and internal documents relating to the activities of the PHC. Reimbursement considerations were key to selling devices to hospitals and selling the procedure to physicians. Publicly, the PHC was "dedicated to raising awareness, particularly among elected Federal healthcare policy makers of the critical importance of pelvic health and to promote healthcare policy makers of the critical importance of pelvic health and to promote education about pelvic health issues. By dispelling myths and misunderstandings, the PHC is committed to improving the quality of life for women with pelvic health disorders." However, internal documents make it clear that the group was formed to increase mesh payments. From Ethicon documents: "This is a coalition which we established at the ACOG meeting this year in Washington with the purpose being to improve hospital reimbursement for pelvic floor procedures which utilize synthetic or autologous products."[68] PHC activities included:

- Publication of an article titled "Options, Best Techniques, and Coding Tips for Pelvic Prolapse Repair" in OB-GYN Management. BSC acknowledges that this "piece, along with the accompanying coding and billing scenarios, was initiated by BSC, AMS, J&J, and Bard through our participation in the Pelvic Health Coalition (PHC).[69]

- Requesting the FDA to delay the 2008 Public Health Notification. The letter appears to be drafted by Industry; however, only physician names appear on the letterhead.[70]

- Petitioning the Center for Medicare and Medicaid Services to give special status to mesh procedures.[71]

- Removing language from an ACOG Technical Bulletin describing mesh procedures as "experimental" (Experimental procedures are typically not paid for by insurance companies and Medicare/Medicaid) [72]

As a result of these efforts, "add-on" codes provided additional reimbursement to physicians for each piece of mesh used. Hospitals could use morbidity codes to obtain higher

[68] ETH.MESH.00136420.

[69] ETH.MESH.00738769; ETH.MESH.01280816; ETH.MESH.01280860; ETH.MESH.00720002.

[70] ETH.MESH.02312097.

[71] CMS-1385-P-15007 (submission receipt, dated August 31, 2007 and accompanying letter); CMS billing; ETH.MESH.00720002.

[72] ETH.MESH.02316434.

DRG[73] reimbursement for mesh operations. In my opinion, these pursuits involved the use of false and misleading information for financial gain and were undertaken with complete disregard for the safety of women who would be implanted with a Prolift device.

Based on my experience, my knowledge of the peer-reviewed medical literature, and my review of internal Ethicon documents, it is my opinion that the risks of the Prolift devices far outweigh any theoretical benefits.

All opinions are provided to a reasonable degree of medical certainty. I reserve the right to amend or supplement this report as new information becomes available. I also reserve the right to adopt all of my opinions in the other reports that I have submitted for the Wave 4 cases.

This 17th day of January, 2017.

Jerry G. Blaivas, MD

[73] DRG: Diagnosis-related groups.

V. FACTS OR DATA CONSIDERED IN FORMING OPINIONS

In addition to the references included herein, an Index is attached hereto and by reference made a part hereof. Please see **Exhibit "C"** attached.

VI. COMPENSATION

Dr. Blaivas' Fee Schedule is attached hereto and by reference made a part hereof. Please see **Exhibit "B"** attached.

VII. LISTING OF CASES IN WHICH TESTIMONY HAS BEEN GIVEN IN THE LAST FOUR YEARS

Merjem Delija v. Neil Sayegh, etc.; index no. 14449/2003

Jose Cuevas v. the Mount Sinai medical Center; Index no. 0017209/2004

Randy Smith, et al. v. Andrew Chan, M.D., et al.; Index No. 024786/2009

Katelyn Vercher, et al. v. Chiari Institute, et al.; 2:09-cv-01751-AKT

Lisa Marie Fontes, et al. v. American Medical Systems, Inc.; 2:12-CV-02472

Debbie Jilovec, et al., v. American Medical Systems, Inc.; 2:12-CV-05561

Joann Serrano, v. American Medical Systems, Inc.; 2:12-CV-3719

Mary Weiler, et al. v. American Medical Systems, Inc.; 2:12-CV-05836

Carolyn F. Smothers v. Boston Scientific Corp.; 2:12-cv-08016

Katherine L. Hall v. Boston Scientific Corp.; 2:12-cv-08186

Julia Wilson v. Boston Scientific Corp.; 2012-02626

Ronda Orozco, et al., v. Boston Scientific Corp.; 2012-03068

Maria Cardenas v. Boston Scientific Corp.; 2012-02912

Diane Albright v. Boston Scientific Corp.; 2012-00909

Bertie Frankum v. Boston Scientific Corp.; 1:15-cv-00091

Teri Matthison, et al. v. Boston Scientific Corp.; 1:15-cv-00092

Jo Huskey, et. al v. Ethicon, Inc.; 2:12-cv-05201

Tonya Edwards, et. al v. Ethicon, Inc.; 2:12-cv-09972

Marty Babcock v. Ethicon, Inc.; 2:12-cv-01052

Daphne Barker, et al. v. Ethicon, Inc.; 2:12-cv-00899

Dorothy Baugher v. Ethicon, Inc.; 2:12-cv-01053

Constance Daino, et al. v. Ethicon, Inc.; 2:12-cv-01145

Lois Durham, et al. v. Ethicon, Inc.; 2:12-cv-00760

Monica Freitas v. Ethicon, Inc.; 2:12-cv-01146

Pamela Gray-Wheeler v. Ethicon, Inc.; 2:12-cv-00455

Beth Harter, et al. v. Ethicon, Inc.; 2:12-cv-00737

Mary Holzerland, et al. v. Ethicon, Inc.; 2:12-cv-00875

Myndal Johnson v. Ethicon, Inc.; 2:12-cv-00498

Debra Lynn Joplin v. Ethicon, Inc.; 2:12-cv-00787

Holly Jones, et al. v. Ethicon, Inc.; 2:12-cv-00443

Beverly Kivel v. Ethicon, Inc.; 2:12-cv-00591

Paul Kirz, et al. v. Ethicon, Inc.; 2:12-cv-00938

Alfreda Lee v. Ethicon, Inc.; 2:12-01013

Angela Morrison, et al. v. Ethicon, Inc.; 2:12-cv-00800

Miranda Patterson v. Ethicon, Inc.; 2:12-cv-00481

Patti Ann Phelps, et al. v. Ethicon, Inc.; 2:12-cv-01171

Maria Eugenia Quijano v. Ethicon, Inc.; 2:12-cv-00799

Jennifer Reyes, et al. v. Ethicon, Inc.; 2:12-cv-00939

Ana Ruebel v. Ethicon, Inc.; 2:12-cv-00663

Denise Sacchetti v. Ethicon, Inc.; 2:12-cv-01148

Stacy Shultis, et al. v. Ethicon, Inc.; 2:12-cv-00654

Cindy Smith v. Ethicon, Inc.; 2:12-cv-01149

Susan Thaman v. Ethicon, Inc.; 2:12-cv-00279

Laura Waynick v. Ethicon, Inc.; 2:12-cv-01151

Rebecca Wheeler v. Ethicon, Inc.; 2:12-cv-01088

Virginia White, el al. v. Ethicon, Inc.; 2:12-cv-00958

Kathleen Wolfe v. Ethicon, Inc.; 2:12-cv-00337

Mary Burnett v. Ethicon, Inc.; 2:12-cv-01795

Reba Crabtree v. Ethicon, Inc.; 2:12-cv-02135

Jean Fleck v. Ethicon, Inc.; 2:12-cv-01681

Janice Shennum v. Ethicon, Inc.; 2:12-cv-01708

Laura Morrison v. Ethicon, Inc.; 2:12-cv-02141

Mary Frances Richard v. Ethicon, Inc.; 2:12-cv-02192

Carla Thorpe v. Ethicon, Inc.; 2:12-cv-02546